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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,761	02/21/2006	Takamasa Watanabe	Q116808	6669

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
11/03/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/568,761	WATANABE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20 and 31-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-20, 31-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 10/06/2010, is acknowledged.

2. Claims 19-20 and 31-37 are pending and under examination a method for improving or treating inflammatory bowel disease (IBD) comprising administering a therapeutic agent comprising an effective amount of anti-CD-81 antibody to a patient in need thereof.

3. The following new ground of rejections are necessitated by the IDS/amendment submitted 10/06/2010.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 19-20, 32 and 35 stand and newly added claims 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S Pat. No. 6,423,501 OR WO/ 98/25647 for the same reasons set forth in the previous Office Action mailed 04/07/2010.

Applicant's arguments, filed 10/06/2010, have been fully considered, but have not been found convincing.

Applicants reiterate that Fleming et al. does not disclose, either expressly or inherently, the specific combination of claim elements claimed by Applicants, i.e., "arranged as described in the claims," as anticipation requires. *In re Arkley*, 455 F.2d 586 (C.C.P.A. 1972). To the contrary, Applicants submit that the selection of the different claim elements from the disclosure of Fleming et al. is impermissible; the record lacks any reference to any specific embodiment within Fleming et al. that unequivocally discloses a method for treating inflammatory bowel disease by administering an antibody against CD81, "arranged as described in the claims." Rather, the rejection is improperly sustained upon the proposition that the disclosure of each claim element individually within different passages describing myriad alternatives for each element - with no pattern of preferences to direct those of skill in the art to the claimed combination of claim elements - is sufficient for anticipation. However, nothing in Fleming et al. directs those of skill in the art to the specifically claimed method; selection of the presently claimed invention requires the picking and choosing of particular claim elements from broad generic disclosures describing myriad alternatives, which is not the standard for anticipation

Applicants submits that while the Examiner attempts to distinguish *Arkley* on its facts, alleging that *Arkley* is inapplicable because the number of possible embodiments was significantly greater, Applicants respectfully point out that neither the Federal Circuit, see e.g., *Net Moneyln, Inc. v. Verisign, Inc*., 2008 U.S. App. LEXIS 21827, 1, 27 (Fed. Cir. 2008), nor the Board of

Patent Appeals and Interferences (BPAI), see e.g., *Ex parte Schulze* (Appeal 2009-013421), has confined Arkley to its facts.

For example, in *Ex parte Schulze*, substantially less embodiments were at issue vis-a-vis *Arkley*. Nonetheless, the Board stated that:

> there is no dispute that [the prior art reference] teaches, at separate locations throughout the reference, each of the elements of the claims. However, [the prior art reference] **does not teach a single composition with each of the claimed elements**, but requires selection of the elements from groups of disclosed compounds ... [t]he instant situation is similar to *Arkley* ... [t]his picking and choosing is not consistent with an anticipation rejection [emphasis added by applicant].

Applicant contends that from Fleming et al., those of ordinary skill in the art would first need to select a particular agent to target CD81 (i.e., an antibody), then select a specific disease to be treated. Nothing in Fleming et al. directs those skill in the art to this combination. At no point does Fleming et al. disclose an embodiment containing each of the claimed elements.

It flows from the foregoing that the relied-upon lists in Fleming et al., when used in combination (as has been done to make the instant rejection), disclose at best no more than a genus of possible treatment methods. While disclosure of a species, if enabled, always anticipates a genus, the converse is not true. See *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991,999 (Fed. Cir. 2006). Specifically, for a genus to anticipate a species, the law recognizes that the genus must be sufficiently limited, or that a pattern of preferences must exist serving to further narrow the genus to a small number of species, so that one of skill in the art would have "at once envisaged" the species. See *In re Petering*, 301 F.2d 676 (C.C.P.A. 1962). In this regard, Applicants respectfully point out that Fleming et al. contemplates a broad genus of possible diseases that can be treated by its inhibition, or by its activation, and a broad genus of agents for effecting such. There is no pattern of preferences in Fleming et al. that serve to narrow the genus of possible treatment methods to disclose the presently claimed invention with sufficient specificity, as anticipation requires.

Applicants concluded that the rejection is improper not only in view of the *Arkley* line of cases, but also in view of relevant law pertaining to anticipation of a species by a genus. Applicants submit that Claims 36 and 37 are not anticipated for the same reasons. In addition, Applicants respectfully submit that Claims 36 and 37 are not anticipated or rendered obvious at least because Fleming et al. is entirely silent as to whether the patients to be treated by such a method have a recognized need for the specific treatment of inflammatory bowel disease that is" associated with shortening of intestinal length, loose stool or diarrhea. See *Jansen v. Rexall Sundown*, 342 F.3d 1329, 1334 (Fed. Cir. 2003), cited in MPEP 2111.02 II. The issue is not whether the antibody of Fleming et al. would inherently treat inflammatory bowel disease (IBD) associated with shortening of intestinal length, loose stool or diarrhea -if attempted- as the rejection posits, but rather, whether Fleming et al. discloses the treatment of inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea. Such is not

disclosed in Fleming et al. Thus, Fleming et al. does not anticipate Claims 36 and 37 for this reason also

However, it appears that Applicant is mischaracterizing the art of Fleming et al. In the instant case, the prior art of Fleming et al explicitly discloses the specific disease name (i.e., IBD) and the specific agent (anti-CD81 antibodies) of the claimed method. Again, it is immediately apparent that the facts in this case do not involve any "need for picking, choosing and combining various disclosures not directly related to each other by the teachings of the cited reference." All the 20 diseases listed by Fleming et al patent are linked by CD81 and the inhibition of inflammatory responses associated with these disorders. Moreover, 20 disorders are very small genus of diseases and the claimed inflammatory bowel disease is taught in the Fleming et al disclosure. In addition, the three agents are directly related to each other in that they all induce CD81-mediated signaling transduction. All that is needed to implement the disclosure of Fleming et al is to treat the inflammatory responses of IBD with anti-CD81 antibody which induces CD81-mediated signal transduction.

The Examiner directs Applicant's attention to the MPEP at 2131.02 which states that "a genus does not always anticipate a claim to a species within the genus, however, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. *Ex parte A,* 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990) (The claimed compound was named in a reference which also disclosed 45 other compounds. The Board held that the comprehensiveness of the listing did not negate the fact that the compound claimed was specifically taught. The Board compared the facts to the situation in which the compound was found in the *Merck Index*, saying that "the tenth edition of the *Merck Index* lists ten thousand compounds. In our view, each and every one of those compounds is 'described' as that term is used in 35 U.S.C. § 102(a), in that publication."). *Id.* at 1718".

Further, *In re Petering*, 166 the Court of Customs and Patent Appeals considered the anticipatory effect of prior art generic formulae that encompassed many specific chemical compounds in addition to the claimed compositions. In *Petering*, the examiner rejected claims to compounds as anticipated by a prior art generic formula, and the Board of Appeals affirmed the rejection. The court found that in addition to the generic formula, the reference disclosed a preferred class of compounds described by the formula. Given that the class was "limited" to "only 20 compounds" and represented only a "limited number of variations" within the generic formula, the court reasoned that "one skilled in this art would, on reading the [reference], at once envisage each member of this limited class, even though this skilled person might not at once define in his mind the formal boundaries of the class as we have done here." Because the author of the reference had "described to those with ordinary skill in this art each of the various permutations here involved as fully as if he had drawn each structural formula or had written each name," the court concluded that the claimed compounds within the preferred class had been "described in a printed publication" within the meaning of § 102.

Fleming et al teachings are distinguished from *Ex parte Schulze*, (Appeal 2009-013421, US Applicant No. 10/451,482), in that Fleming et al references explicitly disclose the specific name of the claimed agent and disease to be treated. Further, *Ex parte Schulze* provides a laundry list of compounds, while in Fleming, the agents are only three. The anticipation rejection in the instant case does not involve hindsight anticipations. All the 20 diseases listed by Fleming et al patent are linked by CD81 and the inhibition of inflammatory responses associated with these disorders. Moreover, 20 disorders are very small genus of diseases and the claimed inflammatory bowel disease is taught in the Fleming et al disclosure. In addition, the three agents are directly related to each other in that they all induce CD81-mediated signaling transduction. All that is needed to implement the disclosure of Fleming et al is to treat the inflammatory responses of IBD with anti-CD81 antibody which induces CD81-mediated signal transduction.

The Examiner disagrees with Applicants that the disclosure of Fleming et al is a generic disclosure, but instead finds that the list of agents which induces CD81-mediated signal transduction is only 3 agents and includes anti-CD81 antibodies. In addition, Fleming et al points that these agents binds to or interacts with CD81 and induces or enhances CD81-mediated signal transduction. As *in re Petering (*a preferred class of compounds described by the formula), Fleming et al discloses that in particular embodiments the antibody is 5D1 or IA12 (see col., 9, II. 65 to col., 10, II. 3 in particular). All the 20 diseases listed by Fleming et al patent are linked by CD81 and the inhibition of inflammatory responses associated with these disorders. Applicants do not dispute that all that was required that it was well within the level of skill of the ordinary artisan to implement the disclosure of Fleming et al to treat the inflammatory response of IBD with anti-CD81 antibodies which induce CD81-mediated signal transduction.

Applicant argues that the instant rejection is further in conflict with the position taken by the Board of Patent Appeals and Interferences in view of *Ex parte Johnson* (Appeal No. 2006-0070) and *Ex parte Vogt* (Appeal No. 2007-3387). In each case, the Board found the anticipation rejections improper because the claim elements had to be individually (and impermissibly) selected from the broad disclosures of the reference patent, where the specification did not direct those of ordinary skill in the art to that specific embodiment vis-a-vis the others. Similarly, nothing in Fleming et al. directs" those of ordinary skill in the art to the combination of elements claimed by Applicants from any other.

However, *Ex parte Johnson* was not written for publication and is not binding precedent of the Board. Similarly, *Ex parte Vogt* is not binding precedent of the Board. The Examiner will not comment on said case law.

6. Claims 19-20, 31-32 and 35 stand and newly added claims 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Curd et al (WO 00/67796) for the same reasons set forth in the previous Office Action mailed 04/07/2010.

Applicant's arguments, filed 10/06/2010, have been fully considered, but have not been found convincing.

Applicants submit that the rejection over Curd et al. is improper at least for the reasons set forth above in response to the rejection over Fleming et al. Indeed, Applicants note that arriving at the claimed invention from the disclosure of Curd et al. requires, as a predicate, first choosing CD81 from the myriad B-cell markers recited in the claims, then selecting the treatment of inflammatory bowel disease. Like Fleming et al., nothing in Curd et al. directs" those of ordinary skill in the art to the combination of elements claimed by Applicants.

Nor is this a case where Curd et al. discloses such a limited genus that the specific method claimed by Applicants is disclosed with "sufficient specificity," as the law requires. Even assuming arguendo that the genera of B-cell markers and diseases, when considered individually are limited, Applicants note that the relevant genus in Curd et al. is the methods disclosed by the combinations of these genera. That is, Claims 2 and 6, taken in combination as the Examiner has done, disclose a genus of 1625 distinct methods, without disclosing any particular species thereof. Applicants respectfully disagree that this constitutes a sufficiently limited genus to compel a finding of anticipation, particularly in view of governing law.

For example, in *In re Petering*, 301 F.2d 676 (C.C.P.A. 1962), the court acknowledged that although a broad genus was disclosed by the allegedly anticipatory reference, the reference identified "specific preferences" which served to narrow the broad disclosure to just a small number of species, of which the later-described species fell within. The court held that this narrow genus of compounds, defined by these "specific preferences," were so few in number (only 22 species) that all the species therein were sufficiently described so as to anticipate those species. Similarly, in *In re Schaumann*, 572 F.2d 312 (C.C.P.A. 1978), the court found that a prior art patent disclosed a limited class of compounds based on a disclosed "preference" for the one variable substituent. The court concluded that the compound in the rejected claim fell within the scope of that limited class of compounds, and thus was anticipated by the prior art patent. Thus, without a pattern of "specific preferences" that serve to narrow a broad disclosed genus to a small number of species, a finding of anticipation is improper. Unlike the prior art at issue in *Petering* and *Schaumann*, Curd et al. fails to disclose or suggest any pattern of preferences that would serve to narrow the broad genus of possible methods encompassed by the claims therein to a small number of species that encompasses Applicants' claimed method. To the contrary, the "pattern of preferences" within Curd et al. is not for an antagonist of CD81, but for an antagonist of CD 19 or CD20.

However, Curd et al lists antagonists binding to a particular cell type, B-cell markers and autoimmune diseases, including the specific anti-CD81 antibody and IBD in claims 2 and 6. All the antagonists taught by Curd et al are directly related by being antagonist to B-cell markers and all the diseases are also directly related by being autoimmune disease. While all experiments in Curd et al are relate to the anti-CD20 antibody rituximab and no experimental detail is provided

on the production and use of anti-CD81 antibodies, however, anti-CD81 antibodies and their use in treating autoimmune diseases including IBD are present in the claims of Curd et al. There is no reason that the ordinary artisan would need to pick and combined unrelated antagonist and diseases, as all that is required by the claims is a administering an anti-CD81 antibody to improve or treat inflammatory bowel disease (IBD). Applicant does not dispute that these antagonists and diseases are related by the B-cell markers and autoimmune diseases. Curd et al is distinguished from *Petering.* Substituent groups in the broad generic formula in Petering represented either hydrogen or alkyl radicals, and an R group containing an OH group. However, the antagonist genus of Curd et al is linked by binding to the surface of B-cell markers and the diseases being autoimmune diseases. As in *Schaumann*, the Curd et al disclosed antagonists which bind to a B cell surface marker, and a disease that being autoimmune disease that each differed only by a single variable, such that only a limited number of antagonists/diseases was encompassed by the implied class.

Contrary to applicant's assertions, as *in re Petering*, the Curd et al teaches a "pattern of preferences" in that the antagonist "binds a B-cell surface receptor" and the disease is "an autoimmune disease". Anti-CD81 antibody was named in Curd et al which also disclosed 25 other antibodies (see claim 2). IBD such as Crohn's disease or ulcerative colitis were named in Curd et al which also disclose 57 other autoimmune diseases (see clam 6). *In re Petering*, the court held that the subgenus, containing only 20 compounds and a limited number of variations (in Curd et al, e.g., B-cell markers/autoimmune disease) in the generic chemical formula, inherently anticipated a claimed species within the genus because "one skilled in [the] art would… envisage each member" of the genus. Thus, a genus anticipates a species if one of ordinary skill in the art is able to "envisage" the species compound within the chemical formula of the genus compound.

Applicants submit that the rejection is also improper because it would require an extensive and undue amount of experimentation for those of skill in the art to specifically link CD81 with inflammatory bowel disease, because Curd et al. provides insufficient direction. Relevant law indicates that prior art containing broad disclosures of alternatives is non-enabling, and thus not anticipatory, where so little guidance is provided to direct those of skill in the art to the later-claimed combination. See, e.g., *Impax Laboratories, Inc. v. Aventis Pharmaceuticals', Inc.*, 545 F.3d 1312 (Fed. Cir. 2008). In *Impax*, the district court held that because the alleged prior art disclosed hundreds of compounds, and several diseases, but did not provide any disclosure that would have directed those of ordinary skill in the art to recognize that riluzole could be used to treat ALS, it would have required "extensive experimentation to link riluzole with the treatment of ALS [the subject matter of the claim at issue]." Similarly, in the instant case, it would require an extensive and undue amount of experimentation for those of skill in the art to have to specifically linked CD81 with inflammatory bowel disease, based on the mere listing of these elements within broad lists of myriad alternatives, because Curd et al. provides no direction or guidance that would lead those of skill in the art to the claimed method. As noted above, Curd et

al. directs those of skill in the art to CD19 or CD20, not CD81. Thus, Curd et al. does not enable the claimed invention, and thus is not anticipatory.

However, Curd et al teach treating autoimmune diseases with antagonists that bind a B-cell surface marker. Curd et al teach that the B-cell markers can include anti-CD81 antibodies and the autoimmune diseases can include inflammatory bowel disease, such as Crohn's disease and ulcerative colitis. It was well within the level of skill of the ordinary artisan to administer the anti-CD81 antibodies to the inflammatory bowel disease subject. The Curd et al teach how to make and how to use. Accordingly, Curd et al is enabling art.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 31 and 33-34 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S Pat. No. 6,423,501 or WO 98/25647 or WO 00/67796, as applied to claims 19-20, 31-32 and 35-37, above, and further in view of and Owens et al (1994) for the same reasons set forth in the previous Office Action mailed 04/07/2010.

Applicant's arguments, filed 10/06/2010, have been fully considered, but have not been found convincing.

As previously noted on the record, and as discussed above, neither Fleming et al., WO 98/25647 nor WO 00/67796 disclose, expressly or inherently, a method of improving or treating inflammatory bowel disease (much less inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea) comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in these references that would incite any expectation of success in performing such a method. Owens et al. fails to rectify this deficiency, being silent as to CD81 and inflammatory bowel disease. Thus, even assuming arguendo these references were combined, those of ordinary skill in the art would not arrive at the presently claimed invention

The Examiner's position with respect to the teachings of `501 patent and `647and `796 publications, is discussed above. It is the Examiner's position that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the anti–CD81 antibody taught by 6,423,501 or WO 98/25647 to Fab or F(ab')2 fragments taught by Owens et al. because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al.*

9. Claims 19, 20 and 31-35 stand and newly added claims 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US. Patent 6,423,501 OR WO 98/25647 for the same reasons set forth in the previous Office Action mailed 04/07/2010.

Applicant's arguments, filed 10/06/2010, have been fully considered, but have not been found convincing.

Applicant asserts that Fleming et al. does not disclose, expressly or inherently, a method of improving or treating inflammatory bowel disease (much less inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea) comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in Fleming et al. that would incite any expectation of success in performing such a method. Applicants respectfully submit that the presently claimed invention is non-obvious, and patentable, for at least this reason.

However, it is the Examiner's position that one of ordinary skill in the art would have had a reasonable expectation of success of improving or treating inflammatory bowel disease according to the teachings of '501 by providing an anti-CD-81 antibody to a patient suffering from this disease inasmuch as the reference discloses that such agents are suitable to treat inflammatory responses associated with disorders such as inflammatory bowel disease and it discloses two specific examples of such anti-CD-81 antibodies. Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process taught by '501 by providing an anti-CD-81 antibody to a patient suffering from inflammatory bowel disease patient by providing specific anti-CD-81 antibodies to such a patient for the expected benefit of improving or treating the painful and distressing condition of inflammatory bowel disease. It would be conventional and within the skill of the art to easily adapt the teachings of the `501 patent to treat inflammatory bowel disease patients with an anti-CD-81 antibody.

10. Claims 19-35 stand and newly added claims 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/67796 to Curd et al for the same reasons set forth in the previous Office Action mailed 04/07/2010.

Applicant's arguments, filed 10/06/2010, have been fully considered, but have not been found convincing.

Applicants submit that Curd et al. does not disclose, expressly or inherently, a method of improving or treating inflammatory bowel disease (much less inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea) comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in Curd et al. that would incite any expectation of success in performing such a method. Applicants respectfully submit that the presently claimed invention is non-obvious, and patentable, for at least this reason.

However, those of skill in the art would have had reason to use the anti-CD81 antibody as a substitute for the improvement and treatment of autoimmune disease including IBD, Crohn's disease and ulcerative colitis because, like the B cell surface marker antagonists taught in Curd, anti-CD81 antibodies bind to B cell surface marker and antagonize its effect would have yielded predictable results of improving or treating of inflammatory bowel disease to one of ordinary skill in the art at the time of the invention. Substituting a known element for another, to yield the known result, is obvious. See KSR, 550 U.S. at 416, 421.

11. Claim 31 stands rejected under 35 U.S.C. 103(a) as being unpatentable over U.S Pat. No. 6,423,501 or WO 98/25647 as applied to claims 19-20 and 32 above and further in view of and Owens *et al* (1994) for the same reasons set forth in the previous Office Action mailed 04/07/2010.

Applicant's arguments, filed 10/06/2010, have been fully considered, but have not been found convincing.

Applicants submit that Fleming et al. does not disclose, either expressly or inherently, a method of improving or treating inflammatory bowel disease (much less inflammatory bowel disease associated with shortening of intestinal length, loose stool or diarrhea) comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in Fleming et al. that would incite any expectation of success in performing such a method. Owens et al. fails to rectify this deficiency, being silent as to CD81 and inflammatory bowel disease. Thus, even assuming arguendo these references were combined, those of ordinary skill in the art would not arrive at the presently claimed invention.

However, it is the Examiner's position that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the anti–CD81 antibody taught by 6,423,501 or WO 98/25647 to Fab or F(ab')2 fragments taught by Owens et al. because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al.*

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 27, 2010

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644